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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,352	05/01/2001	Steven L. Stice	P 0280611	3443

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n N .	Applicant(s)	
	09/845,352	STICE ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE S MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,15-25,33-35 and 47-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,15-25,33-35 and 47-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 May 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's arguments filed February 6, 2003 in paper no. 6 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1-6, 15-25, 33-35 and 47-55 are pending.

Applicant is advised that their drawings/figures are not suitable for issue.

The specification contains references to U.S. Patent Application Ser. No's. These should be converted to U.S. Patent No. went appropriate. See page 21, line 3 as an example. Applicant should review the specification for further errors.

The amendments to the claims have overcome the rejection of claims 18-25 under 35 U.S.C. 112, second paragraph.

The amendments to the claims have overcome the rejections made under 35 U.S.C. 102(b) made in the previous office action.

Claim 55 is objected to as depending from canceled claim 36. For purposes of this examination, claim 55 is being examined as an independent claims with the limitations of claims from which it depends.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 15-17, and 47-54 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record presented in the office action mailed August 6, 2002, in paper no. 3.

The claims are drawn to methods of treating a patient with Parkinson's disease or a Parkinson's-like disease comprising administering to or transplanting dopamine cells from a

cloned ungulate, a method of treating Parkinson's Disease or a Parkinson's-like disease comprising administering to or transplanting into a therapeutically effective amount of cloned, transgenic fetal dopamine cells, a method of treating a patient with Parkinson's or a Parkinson's-like disease comprising transplanting a therapeutically effective amount of a cloned fetal dopamine neuronal cell where the dopamine cell is isolated from a fetus produced by nuclear transfer of a differentiated donor ungulate cell, a method of using an ungulate fetal dopamine neuronal cell like to treat Parkinson's Disease or a Parkinson's-like disease, wherein the cell line is obtained from a cloned fetus produced by nuclear transfer from a differentiated cell propagated in culture, a method of treating Parkinson's disease comprising inserting a donor ungulate cell or nucleus into an enucleated oocyte, isolating at least one fetal dopamine cell or mesencephalic tissue from at least one fetus, transplanting said dopamine cells or mesencephalic tissue in to the brain of patient. The elected group is to methods of treating Parkinson's disease.

The claims are not enabled because at the time of filing neither the art nor the specification provided guidance that transplanting a cell or tissue from a cloned ungulate into an unrelated species would provide a treatment effect. The specification does not provide guidance for the inhibition of hyperacute rejection of xenogeneic transplanted cells. As for the cloning of ungulates from adult tissues, applicant has only enabled cloning by using a cell that has been expanded in culture, that is, a cell undergoing rapid cell division.

As a first point, the examiner agrees with applicant's arguments in-part. The correction of rotational turning in the Parkinsonian rat model by the implantation of bovine mesencephalic tissue is sufficient to indicate a therapeutic effect. However, the problem with this showing is that its application to other animal species is unpredictable.

Applicant argues that the use of immunosuppressives is routine in the art of transplantation therapy, and could be used if only to supply the temporary relief of

symptoms. The examiner, however, is not persuaded by this argument as the breath of the claims encompasses the transplantation of ungulate tissue between discordant species, species that develop a hyperacute rejection of the transplanted tissues. Cyclosporin or similar immunosuppressive drugs do not suppress Hyperacute rejection. In fact, there is no known means through which to suppress an hyperacute rejection.

Applicant argues that the specification teaches that claimed method is uniquely suited to permit one to perform extensive genetic modifications of the cells, and the cells be rejuvenated such that they have an enhanced proliferative lifespan by the nuclear transfer procedure. The examiner does not find this argument persuasive because it is not clear how the increased proliferative life span of a cell from a cloned animal affects the claimed invention. The specification does not disclose genetic modifications in a cell from an ungulate produced by nuclear transfer, isolating a cell from the cloned ungulate, and then performing genetic modification of that cell. All the examiner can find is direction to modify cells first and use the nuclei of those cells in nuclear transfer procedures. How an extended cell life-span affects this method requires explanation. Further, the examiner cannot find anything in the specification about the extended life span. Applicant is requested to refer to specific teachings by page and line number. In fact, the response makes several references to what the specification teaches but applicant does not cite any particular places where these teachings can be found. Applicant is requested to always provide the citations for any specification teachings referred to.

Applicant argues that the skilled artisan could have followed the teachings of the specification and knock out thpse genes encoding proteins responsible for rejection of transplanted organs or tissues. Applicant argues that Phelps successfully cloned α-1,3-galactosyltransferase-deficinet pigs by using somatic cell nuclear transfer similar to those presented in the present disclosure. Applicant argues that similarly other proteins that

stimulate immune rejection could also be knocked out. These arguments are not found persuasive.

While the examiner can find specific mention in the specification to disrupt the gene for α-1,3-galactosyltransferase, the examiner cannot find specific direction to disrupt the gene in fibroblasts, or any of the specific methodology used by Phelps (specification pages 37-38,bridg. parag.). Phelps teaches the production of pigs lacking α-1,3-galactosyltransferase by a double knock out procedure, using fibroblasts from a pig fetus heterozygous for the disruption, as an example. Dai also discloses methodology not disclosed in the present specification. Dai teaches that vectors comprising isogenic DNA was used to disrupt the gene for α-1,3-galactosyltranferase. Further, Phelps state that complete removal of the α-1,3-galactosyltransferase gene combined with transgenic expression of complement regulatory proteins should prevent HAR of pig xenografts (page 254, col. 1, parag. 1, lines 1-4). This is clear evidence that Dai did not regard the heterozygous pig disclosed to be sufficient for reduction HAR. Thus, neither Phelps nor Dai support applicant's allegations that the specification enables the production of knock out pigs or other animals.

Applicant argues that a claimed therapeutic method need not satisfy all of the safety requirements of the FDA in order to comply with enablement.

The examiner would like to point out to applicant that this was not and is not now a basis for the enablement rejection. Applicant is encouraged by the examiner to identify where issues of safety were raised in this record. Prosecution would be better served if applicant would address the rejections of record rather than bring in imagined rejections.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-25 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lopez-Lozano (1987) Society for Neuroscience Abstracts 13, page 513, abs. 141.7.

Lopez-Lozano teaches bovine ventral mesencephalic cells (). These cells are inherently differentiated and dopamine neuronal cells. That many mesencephalic cells were isolated metes the limitation of "cell line." "Clonal" pertains to a method of making the cells, and does not provide distinguishing characteristics to the cells of Lopez-Lozano. Thus, Lopez-Lozano clearly anticipates the claimed invention.

> e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 33-35 and 55 remains rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent 6,294,383 B1 issued September 25, 2001 (Isacson) for reasons of record presented in the office action mailed August 6, 2002 in paper no. 3.

Isacson teaches pig mesencepahlon cells that have been genetically modified by an insertion of a DNA sequence to express a foreign molecule (col. 18, line 66 to col. 19, line 10 and col. 22, lines 34-39). Isacson states that the age of porcine development is between about 20 and 50 days, and has taken form in that specific tissues can be identified and isolated (col. 14, lines 38-46). This encompasses the definition of "fetus" given in the specification: "after it has taken form in the uterus (specification, page 44, lines 1-2). Thus Isacson clearly anticipates the claimed invention.

Applicant argues that the cells taught by Isacson do not have the inherent property of an extended life-span as those taught in the specification. This argument is not persuasive.

Whether or not applicant's cells have a longer life-span is not relevant because the limitation is not in the claim. If applicant's cells have a new property, then that property must be in the claim or the art stands. A new method of making an old product does not

make the product made by the new method patentably distinct unless there is a patentably distinction between them. If the patentable distinction is not in the claim, the art stays. Further, discussion of an increased proliferative life-span is not in the present specification. Any argument of unexpected results is therefore not available to applicant. Applicant has not pointed to any place in the specification were there are references to extended life spans of cells. Applicant is invited to do so.

Claims 1-6, 15-17, and 47-54 are free of the art. At the time of filing the prior did not teach methods of treating Parkinson's disease, methods of using a fetal dopamine neuronal cell for transplantation purposes to treat a patient with Parkinson's disease where the at least one cell or tissue is obtained from a cloned ungulate animal or embryo made by nuclear transfer using a differentiated cell that had been propagated in culture.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
March 22, 2003